UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/519,330	04/25/2005	Peter Carmeliet	50304/056001	3636

21559 7590 10/17/2006

CLARK & ELBING LLP
101 FEDERAL STREET
BOSTON, MA 02110

EXAMINER	
DEBERRY, REGINA M	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 10/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/519,330	CARMELIET ET AL.	
	Examiner	Art Unit	
	Regina M. DeBerry	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 August 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,10,11 and 13-18* is/are pending in the application.

4a) Of the above claim(s) *14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,10,11,13 and 15-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Status of Application, Amendments and/or Claims

The amendment filed 03 August 2006 has been entered in full. Claim 9 was cancelled. New claims 15-18 were added. Claims 16-18 are drawn to a method for suppressing bone resorption in a bone resorption disorder said method comprising contacting an osteoclast cell with an antagonist of placental growth factor that inhibits bone turnover activity of the osteoclast cell so that bone resorption in the bone resorption disorder is suppressed. The Examiner understands claims 16-18 to encompass both an *in vitro* and *in vivo* method.

Claims 1, 10, 11, 13 , 15-18 are under examination.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Information Disclosure Statement

The information disclosure statement(s)(IDS) filed (03 August 2006) was received and comply with the provisions of 37 CFR §§1.97 and 1.98. It has been placed in the application file and the information referred to therein has been considered as to the merits.

Withdrawn Objections And/Or Rejections

The specification is in compliance with 37 CFR 1.821-1.825 of the Sequence Rules and Regulations.

The rejection to claims 1 and 10 under 35 U.S.C. 112, second paragraph, as set forth at pages 4-5 of the previous Office Action (06 February 2006), is *withdrawn* in view of the amendment (03 August 2006).

The objection to claims 11 and 12 under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim, as set forth at page 5 of the previous Office Action (06 February 2006), is *withdrawn* in view of the amendment (03 August 2006) regarding claim 12 and Applicant's arguments regarding claim 11.

The rejection to claims 11 and 13 under 35 U.S.C. 103(a) as being unpatentable over Niida *et al.* (Journal of Experimental Medicine Vol. 190/2:293-298, 1999), is *withdrawn* in view of Applicant's argument regarding osteoporosis, *not* mechanism of bone resorption (03 August 2006). Please see maintained 35 U.S.C. 103(a) rejection.

Claim Rejections - 35 U.S.C. § 103(a)

Claims 1, 10 remain rejected and new claims are rejected for the same reasons under 35 U.S.C. 103(a) as being unpatentable over Niida *et al.* (Journal of Experimental Medicine Vol. 190/2:293-298, 1999). The basis for this rejection is set forth at pages 5-7 of the previous Office Action (06 February 2006).

Applicant argues that the Examiner provides no indication or reference demonstrating that the underlying mechanism of bone resorption in osteoporosis is comparable to the pathway studied by Niida *et al.* or that blocking of PIGF activity would have the same effect as direct VEGF inhibition using anti-VEGF antibodies. Applicant argues that the inverse reasoning of the Examiner would imply that the excessive osteoclast activity in osteoporosis is attributable to excessive VEGF activity, which is not suggested or demonstrated by Niida *et al.* Applicant argues that while Niida *et al.* demonstrate that VEGF can play the role of M-CSF in osteoblast recruitment, this in no way implies that the inverse is true, i.e. that inhibitors of VEGF activity can abrogate the eventual effects of e.g. excessive M-CSF. Applicant argues that there is no indication in Niida *et al.* that the observed effect of VEGF antibodies on op/op mice can also be obtained by PIGF antagonist.

Applicant's arguments have been fully considered and are *deemed partly persuasive* regarding osteoporosis but not the mechanism of bone resorption. Niida *et al.* do not teach osteoporosis. However, claims 1, 10, 15, 16, 17 are drawn to a method for **suppressing bone resorption comprising administering an antagonist of placental growth factor**.

Niida *et al.* teach that mice with osteopetrosis (op/op mice; phenotype is abnormally dense bone) have a severe deficiency of osteoclasts. Bone resorption is bone loss due to increased osteoclast activity. Niida *et al.* teach that M-CSF induced bone resorption in op/op mice. Niida *et al.* clearly teach that VEGF can substitute for

M-CSF in the support of bone resorption and thus VEGF induces bone resorption in op/op mice. Niida *et al.* teach that injection of anti-VEGFR-1 antibody decreased osteoclast (Table II)(applies to new claims 16 and 17). Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Niida *et al.* by administering antibodies against VEGFR-1 (to a subject or osteoclast cells) to suppress bone resorption with a reasonable expectation of success. The motivation and expected success is provided by Niida *et al.* who teach that mice with osteopetrosis (i.e. increased bone density) have a severe deficiency of osteoclasts. VEGF *induced* osteoclastic bone resorption (i.e. low bone density) and that antibodies made against VEGFR-1 *decreased* osteoclast (i.e. suppress bone resorption). Niida *et al.* use an animal model, so it would be obvious to employ those methods in humans. Lastly, the Niida reference does not have to teach that blocking PIGF activity would have the same effect as direct VEGF inhibition using anti-VEGF antibodies. The instant claims do not recite PIGF. The instant claims are broadly drawn to administering an antagonist of placental growth factor (claims 1 and 16) wherein said antagonist is selected from the group consisting of small molecules binding on VEGFR-1 (claims 10 and 17). The scientific reasoning and evidence as a whole indicates that the rejection should be maintained.

NEW CLAIM REJECTIONS/OBJECTIONS

Claim Rejections-35 U.S.C. § 112, First Paragraph, Written Description (New Matter)

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 10, 11, 13, 15-18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This is a new matter rejection. The specification as originally filed does not provide support for the invention as now claimed: "characterized by increased bone turnover" and "suppress said bone turnover" (claim 1) "...inhibits bone turnover activity of the osteoclast cell" (claim 16).

Applicant's amendment, filed 03 August 2006, asserts that no new matter has been added and directs support to paragraphs 4 and 61-68 of US 2005/0175609 A1 for the written description for the above-mentioned "limitations". The wording or connotation of the instant claims is not readily apparent from said sections.

The specification as filed does not provide a written description or set forth the metes and bounds of this "limitations" for the instant methods encompassing the above-mentioned "limitations" as they are currently recited. The instant claims now recite limitations which were not clearly disclosed in the specification as filed, and now change the scope of the instant disclosure as-filed.

Applicant is required to cancel the new matter in the response to this Office action. Alternatively, Applicant is invited to provide specific written support for the "limitations" indicated above or rely upon the limitations set forth in the specification as filed.

Claim Rejections - 35 U.S.C. § 112, Second Paragraph

Claims 1, 10, 11, 13, 15-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 16 recite the limitation "bone turnover" and "bone turnover activity" It is unclear what is meant by "bone turnover" and the instant specification fails to define bone turnover. Would bone turnover mean an increase, decrease or equal amount of bone formation or bone destruction?

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Regina M. DeBerry whose telephone number is (571) 272-0882. The examiner can normally be reached on 9:00 a.m.-6:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda G. Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

RMD
10/12/06

Marianne P. Allen

MARIANNE P. ALLEN
PRIMARY EXAMINER 10/13/06

AU 1647